510(k) SUMMARY

MAY 3 1 2005

"This summary of 510(k) safety and effectiveness information is being submitted in accordance with the requirements of SMDA 1990 and 21 CFR 807.92."

THE ASSIGNED 510(K) NUMBER: K043067

SUBMITTED BY:

BioArray Solutions, Ltd.
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Warren, NJ 07059
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CONTACT PERSON:

Kevin Wyckoff
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DATE OF PREPARATION: April 4, 2005

DEVICE NAME: ENA IgG BeadChip™ Test System on the Array Imaging System (AIS 400)

CLASSIFICATION NAME: Antinuclear antibody immunological test system (21 CFR 866.5100)

PREDICATE DEVICE: ENA IgG ImmuStrip™ Test System
Distributed by SLR Research Corporation
Cleared on April 8, 1995 under document number K964787 by Mardx Diagnostics.

INTENDED USE

The BioArray Solutions ENA IgG BeadChip™ Test System is intended for use in testing human serum for the presence of human IgG class antibodies to six extractable nuclear antigens, SSA, SSB, Sm, Sm/RNP, Scl-70, and Jo-1. The presence of these autoantibodies can be used in conjunction with clinical findings and other laboratory tests to aid in the diagnosis of systemic lupus erythematosus, Sjögren's syndrome, scleroderma and myositis. This ENA IgG BeadChip is for use with Array Imaging System 400 (AIS400). This test is for in vitro diagnostic use.

DEVICE DESCRIPTION

The ENA IgG BeadChip™ Test System is a randomly encoded microarray-based immunoassay for antibodies to extractable nuclear antigens. The device is designed to detect IgG class antibodies in human serum to six extractable nuclear antigens: SSA, SSB, Sm, RNP/Sm, Jo-1, and SCL-70. Each antigen is covalently immobilized to a spectrally distinguishable bead type. A pool of bead types is constructed by mixing all of the bead types of interest including antigen beads, positive control beads, negative control beads, and system control beads. The bead mixture is immobilized as a BeadChip™ microarray on a silicon chip allowing for the simultaneous detection of the auto-antibodies of interest by the AIS 400.

The ENA IgG BeadChip™ Test System kit will contain adequate reagents for 96 assays.

Patient samples are diluted prior to incubation with the BeadChip microarray. If ENA specific antibodies are present in the sample, they will bind to the immobilized antigen on one or more bead types. After washing the unbound serum from the BeadChip, Alexa-Fluor 647 conjugated goat anti-human IgG is added to the BeadChip and briefly incubated. After removing unbound detection conjugate, the BeadChip is imaged with the Array Imaging System 400 (AIS 400) to measure the fluorescent signal associated with the conjugate bound on individual beads. The average signal intensity, coefficient of variance of the intensities, and the number of beads measured for each type is determined and reported. The ENA Analysis program imports the instrument results, assesses the validity of the internal controls, and generates test results.

CHARACTERISTIC COMPARISON TO PREDICATE DEVICE

This ENA IgG BeadChip™ Test System is substantially equivalent in principle and clinical performance to the currently marketed ENA IgG ImmuStrip™ Test System marketed by SLR Research for the detection of extractable antinuclear antibodies. Similarities and differences between the procedures and ENA IgG test kits are described in Table 1.

Table 1 - Comparison with Predicate

DEVICE	PREDICATE
A. Similarities	
Intended Use . The BioArray Solutions ENA BeadChip™ is intended for use in testing human serum for the presence of human IgG class antibody to extractable nuclear antigens (ENA): SSA, SSB, Sm, Sm/RNP, Scl-70, and Jo-1, as an aid in the diagnosis of autoimmune diseases, such as systemic lupus erythematosus, Sjogren's syndrome, sclerodema, and myositis. This test is for *in vitro* diagnostic use.	The SLR ENA IgG Immustrip™ Test System is intended for use in testing human serum for the presence of human IgG to extractable nuclear antigens, as an aid in the diagnosis of autoimmune disease, such as systemic lupus erthematosus, Sjögren's syndrome, sclerodema, and myositis.
Assay type – Immunoassay	Immunoassay
Antigens – SSA, SSB, Sm, Sm/RNP, Scl-70, Jo-1	SSA, SSB, Sm, Sm/RNP, Scl-70, Jo-1
Reporter conjugate – Alexa Fluor 647	Alkaline Phosphatase
Assay Format – Qualitative	Qualitative
Sample Type – Serum	Serum
B. Differences	
Substrate – Microparticle	Strip
Incubation Time – 30/15 minutes	30/30/15 minutes
Method of Detection – Fluorometer	Visual

NON-CLINICAL PERFORMANCE DATA.

Non-clinical performance data has been submitted to address the following aspects:

Performance comparison study to predicate device
Reproducibility study: over-time, operator-to-operator, and site-to-site comparison.
Normal range and cutoff determination and analytical sensitivity.
Cross-reacting and interference substances

Expiry date is two weeks from date of manufacture.

SUMMARY OF PERFORMANCE DATA AND CONCLUSION.

A summary of the method comparison study results is listed in Table 2. The data submitted in this 510(K) Premarket Notification supports the finding that this product is substantially equivalent with respect to the intended use, assay principle, and safety features to the legally marketed predicate device. Therefore, we believe that this device meets the requirement for a "Substantial Equivalence" decision in accordance with the 510(k) guidelines.

Table 2 - Summary of Method Comparison Study Results

Predicate/ BeadChip	POS/POS	NEG/NEG	POS/NEG	NEG/POS	EQU/ND	Total	% Postive Agreement	% Negative Agreement
SSA	47	159	2	10	11	229	95.9	94.1
SSB	21	195	0	8	5	229	100.0	96.1
Sm	48	156	1	10	14	229	98.0	94.0
RNP/Sm	50	155	0	14	10	229	100.0	91.7
Jo-1	21	204	0	1	3	229	100.0	99.5
SCL-70	31	183	3	2	10	229	91.2	98.9

SSA		BeadChip				% Positive Agreement	% Negative Agreement	% Total Agreement
		POS	NEG	EQU	sub-total			
Predicate	POS	47	2	1	49	95.9%	94.1%	94.5%
	NEG	10	159	8	169			
	ND	1	1			(47/49)	(159/169)	(206/218)
	sub-total	57	161		218			

SSB		BeadChip				% Positive Agreement	% Negative Agreement	% Total Agreement
		POS	NEG	EQU	sub-total			
Predicate	POS	21	0	0	21	100.0%	96.1%	96.4%
	NEG	8	195	5	203			
	ND	0	0			(21/21)	(195/203)	(216/224)
	sub-total	29	195		224			

Sm		BeadChip				% Positive Agreement	% Negative Agreement	% Total Agreement
		POS	NEG	EQU	sub-total			
Predicate	POS	48	1	0	49	98.0%	94.0%	94.9%
	NEG	10	156	13	166			
	ND	1	0			(48/49)	(156/166)	(204/215)
	sub-total	58	157		215			

Sm/RNP		BeadChip				% Positive Agreement	% Negative Agreement	% Total Agreement
		POS	NEG	EQU	sub-total			
Predicate	POS	50	0	0	50	100.0%	91.7%	93.6%
	NEG	14	155	9	169			
	ND	1	0			(50/50)	(155/169)	(205/219)
	sub-total	64	155		219			

Jo-1		BeadChip				% Positive Agreement	% Negative Agreement	% Total Agreement
		POS	NEG	EQU	sub-total			
Predicate	POS	21	0	0	21	100.0%	99.5%	99.6%
	NEG	1	204	3	205			
	ND	0	0			(21/21)	(204/205)	(225/226)
	sub-total	22	204		226			

SCL-70		BeadChip				% Positive Agreement	% Negative Agreement	% Total Agreement
		POS	NEG	EQU	sub-total			
Predicate	POS	31	3	9	34	91.2%	98.9%	97.7%
	NEG	2	183	1	185			
	ND	0	0			(31/34)	(183/185)	(214/219)
	sub-total	33	186		219			

Reproducibility Studies –

Day to day reproducibility. The day-to-day reproducibility study was conducted with a pooled positive sample (PDP) containing antibodies to SSA, SSB, Sm, Sm/RNP, Jo-1, and SCL-70 and a pooled normal serum sample (PNS). The ENA IgG BeadChip assay was performed in duplicate for ten consecutive days for a total of twenty runs per sample using three lots of BeadChips. The pooled positive and negative controls were prepared, aliquoted, and stored in a –20°C freezer. A new aliquot was used each day to prepare fresh dilutions. The three lots of BeadChips were manufactured from three independently coupled ENA bead libraries.

The results for the pooled positive sample are reported by antigen, including the mean of the relative activity (RA), standard deviation (SD), and the coefficient of variance (CV) for each lot (intra-lot reproducibility) and the MEAN, SD, and CV of relative activity of all three lots (inter-lot reproducibility). The RA is the ratio between the antigen Normalized Intensity (NMI) and the lot specific cutoff multiplied by 100. Please refer to the Normal Range/Cutoff section in the original submission for further information regarding the cutoff values.

Negative sample were studied and the results were acceptable

Table 3 - Day to Day Reproducibility – Pooled Positive Sample

RELATIVE ACTIVITY (RA)			SSA	SSB	Sm	RNP/Sm	Jo-1	SCL-70
INTRA-LOT 10-DAY REPRODUCIBILITY	Lot-A (n=20)	MEAN	826.1	423.4	661.1	1016.0	458.6	123.3
		SD	92.5	50.7	78.6	125.3	62.2	14.0
		CV(%)	11.2	12.0	11.9	12.3	13.6	11.3
	Lot-B (n=20)	MEAN	890.3	435.4	777.6	1198.9	549.8	135.3
		SD	76.1	64.4	123.3	120.1	69.1	18.6
		CV(%)	8.5	14.8	15.9	10.0	12.6	13.7
	Lot-C (n=20)	MEAN	776.5	442.7	751.1	1115.6	522.8	136.3
		SD	56.4	37.4	87.7	88.8	54.7	15.0
		CV(%)	7.3	8.4	11.7	8.0	10.5	11.0
INTER-LOT	Lot-A,B,C (n=60)	MEAN	831.0	433.9	730.0	1110.2	510.4	131.6
		SD	88.6	51.7	109.0	133.9	72.4	16.8
		CV(%)	10.7	11.9	14.9	12.1	14.2	12.7

Operator-to-operator reproducibility. The operator-to-operator reproducibility was conducted with the pooled positive control, the pooled negative control, and ten disease positive samples. Two researchers performed the ENA IgG BeadChip assays in duplicate. The results are summarized in Table 4, including the mean, standard deviation, and CVs of the relative activity. The CVs were less than 10% for all positive signals; PNS-10 is a pooled negative control and the CV for the weak nonspecific signals for each antigen are much higher compared to disease positive markers.

Table 4 - Operator to Operator Reproducibility

Sample ID	Marker	$Mean_{RA}$	SD_{RA}	CV (%)
AAB206	Sm	312.2	29.7	9.52
AAB206	Sm/RNP	594.1	44.4	7.47
AAB237	Sm/RNP	512.9	40.3	7.86
AAB241	SSA	848.3	61.8	7.28
AAB266	SSA	860.8	35.3	4.10
AAB266	SSB	341.8	12.3	3.59
AAB273	SSB	612.8	33.3	5.43
AAB293	SCL-70	90.8	7.6	8.42
AAB297	SCL-70	111.4	9.5	8.50
AAB313	Jo-1	281.0	24.4	8.68
AAB315	Jo-1	262.8	14.0	5.32
AAB376	Sm	401.7	37.8	9.42
PDP-30	SSA	352.6	22.7	6.44
PDP-30	SSB	218.1	10.3	4.70
PDP-30	Sm	419.0	9.3	2.23
PDP-30	Sm/RNP	596.5	5.7	0.95
PDP-30	Jo-1	280.2	25.4	9.05
PDP-30	SCL-70	76.4	2.9	3.77
PNS-10	SSA	7.4	9.4	127.18
PNS-10	SSB	3.8	2.6	67.82
PNS-10	Sm	13.3	3.0	22.74
PNS-10	Sm/RNP	28.3	6.5	23.12
PNS-10	Jo-1	14.2	4.0	28.25
PNS-10	SCL-70	16.4	1.9	11.83

Note:
1) Two researchers performed the assay in duplicate, separately (4 runs in total).
2) PNS-10: 1:10 diluted pooled normal serum sample
3) PDP-30: 1:30 diluted pooled disease positive sample

Site to site reproducibility. A site-to-site reproducibility study was performed to assess the assay variability between sites, instruments, and operators. Identical serum samples (commercially obtained) were provided to the three testing sites for on-site testing. A histocompatibility and immunocompatibility laboratory holding both CLIA and ASHI certifications was used as one of the testing sites. The second site was a CLIA certified laboratory specializing in providing diagnostic services related to women's health. BioArray Solutions in-house facilities were used for the third site. These samples were randomly encoded to eliminate any references to identity or diagnosis prior to distributing the samples to the investigational sites. A total of 176 samples comprised of 52 normal samples and approximately 25 positive samples for each antigen were used. A total of 192 samples were run at each site. Ten samples were excluded due to specimen control failure at one or more sites and one sample was excluded due to a sample preparation error. Results for two samples for the Scl-70 marker were excluded due to cluster QC failure at one site. These samples were not repeated at that site.

Comparative analysis of the results obtained from two sites showed that the total agreement of positive/negative calls between two sites for SSA, SSB, Sm, Sm/RNP, JO-1, and SCL-70 is 97.2%, 95.6%, 96.7%, 90.6%, 97.2% and 96.1% respectively.

Table 5 - Three Site Comparison of 181 Assays including Positive and Negative Controls

	+/+/+	-/-/-	?/?/?	-/?	+/?	+/-	Total #	Total Agreement (%)
SSA	38	138		3	2		181	97.2
SSB	35	137	1	5	2	1	181	95.6
SM	40	135		5	1		181	96.7
RNP/Sm	38	125	1	15	1	1	181	90.6
Jo-1	37	138	1	3	1	1	181	97.2
SCL-70	27	144	1	5	2		179	96.1

Note: (+) Positive (-) Negative (?) Equivocal

Normal Range, Cutoff, and Analytical sensitivity

Normal range and cutoff. To determine the normal range for each antigen in the ENA IgG Beadchip assay, one hundred thirty normal samples from healthy, asymptomatic human subjects were assayed. The mean and standard deviation of the relative activity (RA) is listed in Table 6. The upper limit of the normal range for each antigen is the mean plus 3~3.5 standard deviations (SD) and the lower limit of the positive range (Cutoff) for each antigen is the mean plus six SD.

Table 6 – Cutoff Determination

(RA Value)	SSA	SSB	Sm	Sm/RNP	Jo-1	SCL-70
Data Points Used	130	130	129	130	130	130
MEAN	5.7	6.0	11.6	16.7	9.2	21.0
SD	15.9	15.5	15.0	14.0	15.1	13.2
Upper limit - normal range	60	60	60	60	60	60
Positive Cutoff	100	100	100	100	100	100

Note: One sample was eliminated for the Sm antigen using the Dixon D/R ratio method (NCCLS C28-A2).

Analytical sensitivity- limit of blank. To determine the sensitivity of the assay, the limit of blank was determined using assays performed with sample diluent in place of serum during the sample incubation. A total of seven assays were performed. The mean and SD of the RA for each antigen are given in Table 7.

Table 7 - Limit of Blank with Sample Diluent

RA	SSA	SSB	Sm	RNP/Sm	Jo-1	SCL-70
Mean	2.4	0.3	2.0	2.9	0.4	1.2
STD	3.6	1.3	0.7	2.9	0.7	0.3
Mean+3xSTD	13.3	4.2	4.1	11.6	2.4	2.1

Cross Reacting Substances

Anti-ds-DNA antibodies. To test whether the anti-ds-DNA antibodies cross-react with the BeadChip ENA antigen panel, six purchased samples characterized by the vendor as positive for anti-ds-DNA were tested side by side with the BeadChip and the predicate device. Both the BeadChip and the predicate detected anti-SSA reactivity in three of the six samples. In addition, two of the three samples positive for anti-SSA also tested positive for anti-SSB antibodies with the BeadChip but not with the predicate. Competitive inhibition assays confirmed that the observed anti-SSA and anti-SSB activity were independent from the anti-ds-DNA antibodies. No cross-reaction was detected from the anti-ds-DNA antibodies.

Rheumatoid Factor (RF). To test whether rheumatoid factor cross-reacts with the BeadChip ENA antigen panel, two purchased samples characterized by the vendor as positive for rheumatoid factor were tested with the BeadChip. One sample showed weak anti-SSA and anti-RNP activities while the other showed no activity to any antigen. The RF samples were spiked into a weak positive control (PDP90) in equal quantity and observed activity was additive. Competitive inhibition assays confirmed that the observed anti-SSA and anti-Sm/RNP activity was independent of the rheumatoid factor activity. No cross-reaction was detected from the rheumatoid factor.

Interference Substances

Hemolytic and lipidemic samples. To investigate the performance of the ENA IgG BeadChip Test System in the presence of potential interferents, a hemolytic sample was identified from the normal samples and a lipidemic sample was identified from the disease samples. These two samples were added at a 1:10 dilution to the pooled positive control. The hemolytic sample did not have significant effect on assay performance, while the lipidemic sample showed apparent interference with the assay, including inhibition of the protein L activity resulting in a chip QC failure. It is recommended that lipidemic samples not be used with the BeadChip.

Additionally, PDP-90 samples were titrated with purified hemoglobin and bilirubin purchased from Sigma to identify the operating range of the assay in the presence of these substances. Bilirubin at concentrations of 10, 20, and 40 mg/dl and hemoglobin at concentrations of 250, 500, and 1000 mg/dl were not found to interfere with the assay within the tested limits.

DEPARTMENT OF HEALTH & HUMAN SERVICES

Public Health Service

Food and Drug Administration
2098 Gaither Road
Rockville MD 20850

MAY 31 2005

BioArray Solutions, Ltd.
c/o Mr. Kevin Wyckoff
Quality Assurance & Regulatory Affairs Manager
35 Technology Drive
Suite 100
Warren, NJ 07059

Re: k043067
Trade/Device Name: ENA IgG BeadChip™ Test System on the Array Imaging System (AIS 400)
Regulation Number: 21 CFR 866.5100
Regulation Name: Antinuclear antibody immunological test system
Regulatory Class: Class II
Product Code: LLL
Dated: November 5, 2004
Received: November 8, 2004

Dear Mr. Wyckoff:

We have reviewed your Section 510(k) premarket notification of intent to market the device referenced above and have determined the device is substantially equivalent (for the indications for use stated in the enclosure) to legally marketed predicate devices marketed in interstate commerce prior to May 28, 1976, the enactment date of the Medical Device Amendments, or to devices that have been reclassified in accordance with the provisions of the Federal Food, Drug, and Cosmetic Act (Act) that do not require approval of a premarket approval application (PMA). You may, therefore, market the device, subject to the general controls provisions of the Act. The general controls provisions of the Act include requirements for annual registration, listing of devices, good manufacturing practice, labeling, and prohibitions against misbranding and adulteration.

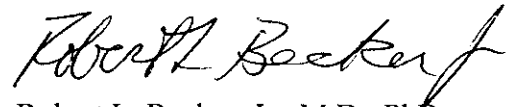
If your device is classified (see above) into either class II (Special Controls) or class III (PMA), it may be subject to such additional controls. Existing major regulations affecting your device can be found in the Code of Federal Regulations, Title 21, Parts 800 to 898. In addition, FDA may publish further announcements concerning your device in the Federal Register.

Please be advised that FDA's issuance of a substantial equivalence determination does not mean that FDA has made a determination that your device complies with other requirements of the Act or any Federal statutes and regulations administered by other Federal agencies. You must comply with all the Act's requirements, including, but not limited to: registration and listing (21 CFR Part 807); labeling (21 CFR Part 801); good manufacturing practice requirements as set forth in the quality

systems (QS) regulation (21 CFR Part 820); and if applicable, the electronic product radiation control provisions (Sections 531-542 of the Act); 21 CFR 1000-1050.
This letter will allow you to begin marketing your device as described in your Section 510(k) premarket notification. The FDA finding of substantial equivalence of your device to legally marketed predicate device results in a classification for your device and thus, permits your device to proceed to the market.

If you desire specific advice for your device on our labeling regulation (21 CFR Part 801), please contact the Office of Compliance at (240) 276-0131. Also, please note the regulation entitled, "Misbranding by reference to premarket notification" (21CFR Part 807.97). You may obtain other general information on your responsibilities under the Act from the Division of Small Manufacturers, International and Consumer Assistance at its toll-free number (800) 638-2041 or (301) 443-6597 or at its Internet address
http://www.fda.gov/cdrh/dsma/dsmamain.html

Sincerely yours,



Robert L. Becker, Jr., M.D., PhD
Director
Division of Immunology and Hematology Devices
Office of In Vitro Diagnostic Device Evaluation and Safety
Center for Devices and Radiological Health

Enclosure

INDICATIONS FOR USE STATEMENT

510(k) Number (if known): K043067

Device Name: ENA IgG BeadChip™ Test System

Indications For Use:

The BioArray Solutions ENA IgG BeadChip™ Test System is intended for use in testing human serum for the presence of human IgG class antibodies to six extractable nuclear antigens, SSA, SSB, Sm, Sm/RNP, Scl-70, and Jo-1. The presence of these autoantibodies can be used in conjunction with clinical findings and other laboratory tests to aid in the diagnosis of systemic lupus erythematosus, Sjögren's syndrome, scleroderma and myositis. This ENA IgG BeadChip is for use with Array Imaging System 400 (AIS400). This test is for in vitro diagnostic use.

(PLEASE DO NOT WRITE BELOW THIS LINE - CONTINUE ON ANOTHER PAGE IF NEEDED)

Concurrence of CDRH, Office of Device Evaluation (ODE)

Prescription Use	X	OR	Over-The-Counter Use
(Per 21 CFR 801.109)			(Optional Format 1-2-96)

Division Sign-Off

Office of In Vitro Diagnostic Device Evaluation and Safety

510(k) K043067